

**MAY 17 2004**

K033747

#### **4.0 510(k) Summary of Safety and Effectiveness**

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: **K033747**

#### **1. Establishment**

Response Biomedical Corp.  
8081 Lougheed Highway  
Burnaby, British Columbia  
Canada, V5A 1W9

Tel: (604) 681-4101  
Fax: (604) 412-9830

Contact: William J. Radvak  
President and CEO

Prepared: November 27, 2003

#### **2. Regulatory Information**

<b>Trade Name:</b>	<b>Response Biomedical Corp. RAMP® CK-MB Assay</b>
<b>Common Name:</b>	CK-MB immunological test system
<b>Classification Name:</b>	CK-MB immunological test system
<b>Regulation Number:</b>	<b>862.1215</b>
<b>Product Code:</b>	<b>JHX</b>
<b>Panel:</b>	<b>Clinical Chemistry</b>

#### **3. Predicate Device**

Immunoassay: Triage Cardiac Panel®; CK-MB Assay (K973126) which is currently being marketed by Biosite Diagnostics, Inc.

Immunoassay: Dimension® RxL Mass Creatine Kinase MB Isoenzyme Flex®, (K970343) which is currently being marketed by Dade Behring Inc.

#### 4. Description of the Device

The RAMP CK-MB Assay is a quantitative immunochromatographic test for the determination of CK-MB levels in EDTA whole blood. Diluted EDTA whole blood is added to the sample well of the Test Cartridge which houses the immunochromatographic test strip. The red blood cells are retained in the sample pad, and the separated plasma migrates along the strip. Fluorescent-dyed latex particles coated with anti-CK-MB antibodies bind to CK-MB, if present in the sample. As the sample migrates along the strip, CK-MB bound particles are immobilized at the detection zone, and additional particles are immobilized at the internal control zone.

The RAMP Reader then measures the amount of fluorescence emitted by the complexes bound at the detection zone and at the internal control zone. Using a ratio between the two fluorescence values, a quantitative reading is calculated.

#### 5. Indication for Use

The RAMP CK-MB Assay is a quantitative immunochromatographic test indicated for use as an in vitro diagnostic product used with the RAMP Clinical Reader to measure CK-MB levels in EDTA whole blood. Measurement of CK-MB aids in the rapid diagnosis of acute myocardial infarction (AMI). The RAMP CK-MB Assay is not intended to monitor reperfusion patients. The RAMP CK-MB Assay is intended to be used only to prioritize patient management for those suspected of AMI.

#### 6. Comparison of Technological Characteristics

The RAMP CK-MB Assay, Triage Cardiac Panel (Triage) - CK-MB; and Dade Dimension RxL (Dimension) Creatine Kinase MB Isoenzyme (CK-MB) Flex Assays are for the quantitative measurement of CK-MB in human whole blood (RAMP and Triage) or plasma (Triage and Dimension). All three immunoassays utilize the binding of CK-MB to specific antibodies and utilize light in their respective detection systems. Both the RAMP and Triage assays measure light production from a fluorescence reaction using a fluorometer while the Dimension measures the amount of colored product produced which is directly proportional to the concentration of CK-MB present in the patient sample. Both the RAMP CK-MB and the Triage CK-MB are quantitative immunochromatographic tests, whereas the Dimension CK-MB test is a sandwich enzyme immunoassay.

#### 7. Summary of Studies

##### PERFORMANCE CHARACTERISTICS

**PRECISION:** The intra-assay and the inter-assay precision of the RAMP CK-MB Assay were determined by one operator assaying duplicates of three standards (7.19, 14.29 and 25.06 ng/mL CK-MB) twice each day over 10 days. The mean, standard deviation and %CV were calculated for the predicted CK-MB at each concentration. Within run precision was 7.7%, 7.8% and 4.8% respectively. Total precision was 8.6%, 8.5% and 6.9% respectively.

**LINEARITY and PERCENT RECOVERY:** CK-MB antigen concentrations of 2.5, 5.0, 10.0, 20.0, 40.0 and 60.0 ng/mL were prepared in normal donor EDTA blood. The linearity and percent recovery were determined by assaying five replicates of each concentration and baseline. The mean, standard deviation and %CV were calculated for the predicted CK-MB at each concentration. Linear regression analysis of actual CK-MB concentration versus expected CK-MB concentration resulted with an  $R = 0.999$  and a slope of 1.05 with an offset of 0.098. The recovery of spiked CK-MB antigen at the six concentrations ranged from 99 to 111% with an average of 106%.

**HOOK EFFECT:** There is no high dose hook effect in the RAMP CK-MB Assay up to the highest level tested (1000 ng/mL CK-MB).

**ANALYTICAL SENSITIVITY:** The lower limit of detection (LLD) is defined as the analyte concentration corresponding to the mean ( $n=20$ ) plus 2 standard deviations of the zero. The LLD is 0.32 ng/mL CK-MB. CK-MB levels in excess of 80 ng/mL are reported as greater than ( $>$ ) 80 ng/mL.

**ANALYTICAL SPECIFICITY:** Potentially cross-reactive substances were evaluated by spiking different concentrations into blood. CK-MM and CK-BB appear to have no significant cross-reactivity with the RAMP CK-MB Assay. HAMA, HAGA, HARA and RhF appear to have limited cross-reactivity with the RAMP CK-MB Assay.

**INTERFERENCE:** Potentially interfering substances were evaluated by spiking different concentrations of potential interferents in blood with CK-MB added. Different blood samples were used for each potential interferent. Interference was evaluated by calculating the CK-MB concentration of potential interferent-spiked blood, expressed as a percentage of the CK-MB concentration of the unspiked (no potential interferent) blood sample. No evidence of cross-reactivity or interference was observed for hemoglobin, triglyceride, bilirubin, cholesterol, or heparin at levels of very high physiological concentrations, up to 2000 mg/dL, 3000mg/dL, 80 mg/dL, 500 mg/dL, and 104 IU/mL, respectively. No trend was observed in the CK-MB predictions as the concentration of potential interferent was increased.

## **CLINICAL PERFORMANCE**

### **EXPECTED VALUES**

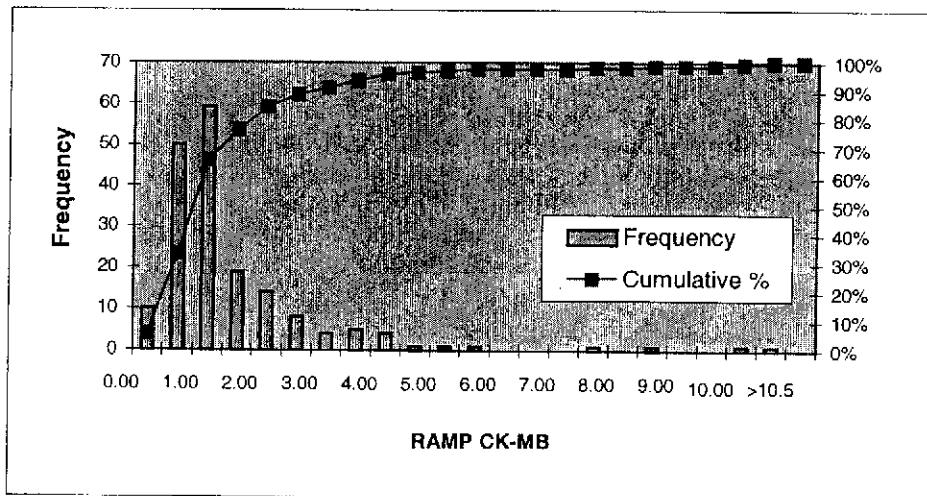
Whole blood samples from 180 healthy individuals (84 males and 96 females) were assayed for Troponin I by the three methods, RAMP, Triage, and Dimension. The lower (LLN) and upper (ULN) limits for normal range were defined as the 5<sup>th</sup> and 95<sup>th</sup> percentile values and are presented in Table 4-1. The RAMP CK-MB normal range distribution is presented in Figure 4-1.

The normal range of the RAMP CK-MB Assay was found to be 0.00 to 3.74 ng/mL in the normal population studied. The Triage system reports values less than 0.8 as " $< 0.8$ " and because of this the normal range of the Triage Troponin I Assay was found to be 0.80 to 4.94 ng/mL in the normal population studied. This is very similar to the normal range described in the Triage CK-MB package insert of  $< 4.3$  ng/mL [1]. Finally, the Dimension normal range was found to be 0.10 to 3.11 ng/mL in the normal population studied. This is very similar to the normal range described in the Dimension CK-MB package insert of 0.00 to 3.6 ng/mL [2]. The data is presented in Table 4-1.

**Table 4-1: Percentile Ranking of Normal Individuals**

	<b>RAMP</b>	<b>Triage</b>	<b>Dimension</b>
<b>Percentile</b>	<b>ng/mL</b>	<b>ng/mL</b>	<b>ng/mL</b>
5 <sup>th</sup> (LLN)	0.00	0.80	0.10
50 <sup>th</sup>	0.78	1.30	0.70
90 <sup>th</sup>	2.87	3.83	2.21
95 <sup>th</sup> (ULN)	3.74	4.94	3.11
97.5 <sup>th</sup>	4.99	8.38	4.88

**Figure 4-1: RAMP Normal Range Distribution**



## PRECISION STUDY

One hundred and eighty-four (184) subjects were enrolled in the Precision Study. Of these, 55 were normal individuals (28 males and 27 females) and 129 were suspected of acute myocardial infarct (AMI) based on the individual hospital criteria (76 males and 53 females). The samples were selected from those obtained during the Method Comparison Study. The samples were stored refrigerated for up to one day between analyses. The data were reviewed and one outlier was removed from the population with suspect AMI. Correlation for CK-MB replicate Result 2 vs Result 1 is presented in Table 4-2.

**Table 4-2: Precision of RAMP CK-MB Assay, Result 1 vs Result 2**

Population	n	Slope y =	Intercept	R <sup>2</sup>	R
Combined Populations,	183	0.989	0.021	0.988	0.993
Patients with suspect AMI	128	0.989	0.051	0.986	0.993
Normal Individuals	55	0.926	0.056	0.920	0.959

#### METHOD COMPARISON

Three hundred and sixty-five (365) subjects were enrolled in the Method Comparison Study. Of these subjects 180 were normal individuals (84 males and 96 females) and 185 were patients suspected of AMI based on the individual hospital criteria (115 males and 70 females). EDTA and heparin whole blood samples were obtained for each of these subjects. All normal subjects were consented. Waste samples were used for the subjects suspected of AMI. An aliquot of whole blood was taken for the RAMP CK-MB Assay and heparinized plasma was prepared for the Triage CK-MB Assay and the Dimension CK-MB assay. The samples were stored refrigerated for up to one day between analysis for the rapid tests. Heparin samples were frozen and sent to a reference lab for the Dimension testing.

Results were compared between the RAMP CK-MB and the Triage CK-MB each to the Dimension CK-MB Assay. The data were winsorized to account for the differing reportable ranges and two outliers were removed from the suspect AMI samples from both the RAMP and Triage analyses. The correlation data is presented for both the RAMP and Triage CK-MB Assays versus the Dimension CK-MB Assay in Table 4-3.

**Table 4-3: Correlation of RAMP and Triage vs. Dimension**

Population	n	Slope y =	Intercept	R <sup>2</sup>	R
<b>RAMP CK-MB Assay</b>					
Combined Normal and Suspect AMI Subjects	363	0.966	0.600	0.972	0.986
Suspect AMI Subjects	183	0.955	1.207	0.967	0.984
Normal Subjects	180	0.978	0.162	0.779	0.882
<b>Triage CK-MB Assay</b>					
Combined Populations	363	1.036	2.204	0.962	0.981
Patients with suspect AMI	183	1.017	3.783	0.963	0.981
Normal Individuals	180	1.124	0.911	0.209	0.457

#### 8. Conclusion

The RAMP CK-MB Assay when utilized with the RAMP Reader is substantially equivalent to other assays currently in commercial distribution for the measurement of CK-MB.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration  
2098 Gaither Road  
Rockville MD 20850

**MAY 17 2004**

Mr. William J. Radvak  
President and CEO  
Response Biomedical Corp.  
8081 Loughheed Hwy.  
Burnaby, British Columbia,  
Canada V5A 1W9

Re: k033747  
Trade/Device Name: RAMP CK-MB Assay  
Regulation Number: 21 CFR 862.1215  
Regulation Name: Creatine phosphokinase/creatine kinase or isoenzymes test system  
Regulatory Class: Class II  
Product Code: JHX  
Dated: March 15, 2004  
Received: March 15, 2004

Dear Mr. Radvak:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

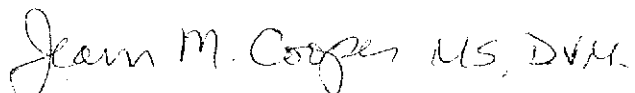
Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

Page 2

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address <http://www.fda.gov/cdrh/dsma/dsmamain.html>.

Sincerely yours,



Jean M. Cooper, MS, D.V.M.

Director

Division of Chemistry and Toxicology

Office of *In Vitro* Diagnostic Device

Evaluation and Safety

Center for Devices and

Radiological Health

Enclosure

## Indications for Use

510(k) Number (if known): K033747

Device Name: RAMP CK-MB Assay

Indications For Use: The RAMP CK-MB Assay is a quantitative immunochromatographic test indicated for use as an in vitro diagnostic product used with the RAMP Clinical Reader to measure CK-MB levels in EDTA whole blood. Measurement of CK-MB aids in the rapid diagnosis of acute myocardial infarction (AMI). The RAMP CK-MB Assay is not intended to monitor reperfusion patients. The RAMP CK-MB Assay is intended to be used only to prioritize patient management for those suspected of AMI.

Prescription Use X (IVD) AND/OR Over-The-Counter Use N/A  
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

---

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

  
Division Sign-Off

Office of In Vitro Diagnostic  
Device Evaluation and Safety

Page 1 of 1

510(k) K033747